

## REMARKS

This is a full and timely response to the Official Action mailed May 12, 2008. This Amendment is timely in view of the Petition for Extension of Time filed concurrently herewith. Reexamination and reconsideration of the rejections set forth therein in light of the following remarks are courteously requested.

The claims have been amended to delete the term “from” in claims 79, 81-83 and 85-86 in order to clarify the meaning of the claims.

The Office Action of May 12, 2008 withdrew the allowability determination of claims 73-76. The Office Action of May 12, 2008 further rejected Claims 79-86 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis for this rejection is that the “term ‘from about’, ‘at least about’ are not defined by the claim...” [Office Action, p. 3]. Applicants respectfully submit that the amendments to the claims set forth above removing the term “from” in claims 79, 81-83 and 85-86 render this rejection moot and respectfully request reconsideration of this rejection in light thereof.

The Office Action of May 12, 2008 also rejected claims 73-78 under 35 U.S.C. §103(a) as being unpatentable over Meybeck et al., US 5,034,228 in view of Sessa et al. JAOCs vol. 69(3) 1992, 209-212 (“Sessa et al.”) and Seiberg et al. J. Invest. Dermatol. 109:370-376 1997 (“Seiberg et al.”). The basis for this rejection was stated as follows:

Meybeck et al., teach treating acne with soya lecithin and tretinoin. It is a known knowledge to one of ordinary skill in the art that soya lecithin is extracted from soybean or soybean powder, absent factual evidence, therefore claims 73-74 and 76-78 are obvious variations of soybean extract...With regard to claim 75, the reference teaches retinol as vitamin A...As to the soybean extract having trypsin inhibitory activity it is known in the art that soy products have varying trypsin inhibitory activity as discussed below by Sessa et al.

Sessa et al teach soy products with varying trypsin activity inhibitor...(the reference used merely to show that soy products do contain trypsin-inhibiting activity). Please note that nondenatured soybean extract encompasses soybean lecithin which in [sic] known in the art to have trypsin activity inhibitor...

Seiberg et al. teach cell death of acne is eliminated by trypsin treatment and that trypsin might increase the therapeutic value of acne treatment and improve skin elasticity while reducing irritating effect. Thus one of ordinary skill in the art would be mo[t]ivated to add a trypsin-inhibiting activity agent to the composition as taught in the prior art...

It would have been obvious to one of ordinary skill in the art to have treated acne with a retinoid compound such as tretinoin and retinol in combination with a soy product having trypsin inhibitor because as taught by Seiberg et al. trypsin increase the

therapeutic value of acne treatment and improve skin elasticity while reducing irritating effect. One of ordinary skill in the art would have been motivated to use a trypsin inhibitor such as a soy extract with either tretinoin or retinol because it is known in the art. [Office Action, pp. 4-5]

Applicants respectfully request reconsideration of the foregoing rejection in view of the ensuing remarks and Declaration of Miri Seiberg, Ph.D. respectfully submitted concurrently herewith ("Seiberg Declaration").

The Meybeck et al. patent relates to "hydrous lipidic lamellar phases or liposomes containing, as an active agent, a retinoid or a structural analogue of retinoid... These compositions are more efficient against acne and less irritant for the skin..." [Meybeck, et al., Abstract]. "Hydrogenated soya lecithin" [Meybeck, et al., col. 8, l. 2] is mentioned as one of the components of a composition for treating acne skin. However, applicants respectfully assert that Meybeck et al. neither suggests nor describes the compositions or methods of applicants' invention.

Meybeck et al. utilizes lecithin in the liposomes described therein to form the lipidic layer portion of the liposomes. Soybeans have a multitude of components, which can be separated out from the natural beans in several ways. Generally, lecithin is removed from the soybeans using organic solvents—these solvents solubilize the lipidic lecithin molecules and separate them from the remainder of the beans. [Seiberg Declaration, ¶¶1, 2] Soy trypsin inhibitor proteins, like other proteins, are not soluble in organic solvents. Moreover, organic solvents tend to denature proteins [Seiberg Declaration, ¶3]. Meybeck et al. nowhere states or suggests that the soya lecithin useful in the liposomes described therein should be processed so as to maintain soy trypsin inhibitory activity nor does it recognize that soy trypsin inhibitory activity is important in enhancing the activity of retinoids against acne. Applicants therefore respectfully submit that Meybeck et al. would not have led one of ordinary skill in the art to the compositions and/or methods of applicants' invention.

Sessa et al. relates to the determination that trypsin inhibitor activity is present in toasted soybean flour. [Sessa et al., p. 784]. Sessa et al. does not remedy the inadequacies of Meybeck et al. in suggesting the compositions and/or methods of applicants' invention to one of ordinary skill in the art at the time of the invention. Nowhere does Sessa et al. indicate that trypsin inhibitor activity is useful in treating skin conditions. Rather, Sessa et al. merely

indicates that there is trypsin inhibitor activity in soybean flour. In fact, Sessa et al. states that trypsin inhibitor activity may be related to negative physical effects in rats fed with toasted soybean flour and that *its presence should be eliminated*:

Since long term rat feeding studies with raw, toasted and overtoasted soybean flour treatments show a linear dose relationship for pancreatic lesion formation (1), our results are consistent with the hypothesis that attributes hyperplasia and tumor formation to the proteinaceous TI's [trypsin inhibitors]. *Methods will be developed to inactivate the protease inhibitors, both in the purified state and in food systems.* [Sessa et al., pp. 787-788] (emphasis added)

Thus, applicants respectfully submit that Sessa et al. would teach away from utilizing soybean extracts containing trypsin inhibitors.

Nor would the Seiberg et al. publication, taken alone or in combination with Meybeck et al. or Sessa et al. have lead one of ordinary skill in the art to the compositions and/or methods of applicants' invention. In fact, applicants respectfully submit that it would have lead *away* from their invention.

The Seiberg et al. publication relates to the use of *trypsin* (as opposed to *trypsin inhibitors*) in inducing desquamation and utriculi-epidermal differentiation in skin:

The pathogenesis of acne vulgaris is multifactorial, resulting from excessive follicular keratinization and sebum production and bacterial proliferation contributing to inflammation. Effective management should be directed to the combination of these four factors. While topical retinoids are considered to be the most effective single comedolytic agent, their clinical efficacy is limited by their irritant effects. Here we show that *the combination of trypsin with suboptimal doses of tRA could lead to a potentially effective comedolytic agent with a lower irritation profile.* [Seiberg, et al., p. 375]. (emphasis added)

Applicants respectfully submit, in view of the foregoing, that Seiberg et al. teaches away from the compositions and methods of applicants' invention. Rather than suggesting that *trans* retinoic acid be combined with *trypsin inhibitor* to treat acne, Seiberg et al. clearly suggests that tRA be combined with *trypsin* to treat acne.

Therefore, if one of ordinary skill in the art were to have read Meybeck et al., Sessa et al. and Seiberg et al. together, applicants respectfully assert that that person would not have been lead to the compositions or methods of applicants' invention. Meybeck et al. mentions a lipidic extract of soy that would most likely *not* contain soy trypsin inhibitor; Sessa et al.

merely states that soy may contain trypsin inhibitory activity, but that it is undesirable; and Seiberg et al. suggests that trypsin, *not trypsin inhibitor*, would be combinable with a retinoid to treat acne. This would have lead to the opposite result than that of the compositions and methods of applicants' invention. In view of the foregoing discussion, applicants respectfully request reconsideration of the rejection of claims 73-78 under 35 U.S.C. §103(a).

The Office Action of May 12, 2008 further rejected claims 79-86 under 35 U.S.C. §103(a) as being unpatentable over Meybeck et al., US 5,034,228 in view of Sessa et al. JAOCS vol. 69(3) 1992, 209-212 ("Sessa et al.") and Seiberg et al. J. Invest. Dermatol. 109:370-376 1997 ("Seiberg et al.") as applied to claims 73-78. The grounds for this rejection were given as follows:

Meybeck teaches 2 g of soy lecithin and 0.1 g of tretinoin which examiner has interpreted to be within the claim invention of 79, 81-83 and 85-86...One of ordinary skill in the art would be motivated to optimize the concentration of the active agents for the treatment of acne because it is known in the art that topical application of the retinoids in the past gave undesirable effects such as irritation...Based on that the determination of a dosage having the optimum therapeutic index is well within the level of the ordinary skill in the art, and the artisan would be motivated to determine the optimum amounts to get the maximum effect of the drug, hence the reference makes obvious the instant invention. [Office Action, p. 6]

Applicants respectfully request reconsideration of the foregoing rejection in view of the ensuing discussion.

As set forth above, Meybeck does not teach or suggest the use of a soy extract containing soy trypsin inhibitory activity. Sessa et al. merely states that certain soybean materials can contain residual trypsin inhibitory activity. Seiberg et al. suggests that trypsin, rather than soy trypsin inhibitor proteins, would be useful in treating acne. These references, taken together or separately, would not have lead one of ordinary skill in the art to the compositions or methods of applicants' invention.

In view of the foregoing discussion, applicants respectfully request reconsideration of the rejection of claims 73-78 under 35 U.S.C. §103(a).

Accordingly, applicants respectfully submit that the above-captioned application is now in condition for allowance. Accordingly, favorable reconsideration of the above remarks and an

early Notice of Allowance are courteously solicited. If the Examiner has any comments or suggestions that could place this application in even better form, the Examiner is requested to telephone the undersigned Attorney at the below-listed number.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 10-0750.

Respectfully submitted,

/Andrea L. Colby/

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